

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 22

REMARKS

This amendment is responsive to the Office Action mailed July 14, 2003 (Paper 11). Original Claims 1-19 are under examination in the present action. Claims 3, 4, 6, 8, and 11 are withdrawn from consideration. Claims 1, 2, 5, 7, 9, 10, and 14-18 stand rejected. Claims 12, 13 and 19 are objected to for being dependent on a rejected base claim.

Applicants have amended claims 1, 9, 10, 15 and 16, canceled claims 17 and 18, and added claims 20 and 21. Applicants respectfully request reconsideration of the pending Office Action, entry of new claims 20 and 21 and allowance of pending claims 1, 2, 5, 7, 9, 10, 14-16, 20 and 21.

1. Applicants acknowledge the Examiner's maintaining of the restriction requirement detailed in the Office Action mailed November 13, 2002 (Paper No. 7). Applicants contend that the Examiner has not established that the present application does not fulfill the requirement as required under PCT Rule 13.2, as adopted by MPEP §1893.03(d). In an effort to advance the prosecution of the instant application, however, Applicants have amended the present application to limit the scope of coverage consistent with the election of Group I as defined in the prior Office Action (Paper No. 7) due to the finality of the restriction requirement.

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 23

2. Applicants contend that the Examiner has applied the incorrect authority in the instant Office Action by withdrawing claims 3, 4, 8 and 11 from consideration. Applicants contend that, since the instant application is an international application, 37 CFR 1.499 should have been applied, not 37 CFR 1.142(b), which is applicable only to national applications. See MPEP §1893.03(d). In an effort to advance the prosecution of this application, however, Applicants have voluntarily withdrawn claims 3, 4, 8 and 11.

3. Claims 1, 2, 5, 7 and 14-18 stand rejected as being drawn to an improper *Markush* group¹. Applicants submit that the *Markush* groups recited in claims 1, 2, 5, 7 and 14-18 are acceptable alternative expressions as provided for by MPEP §2173.05(h). The members of the subject *Markush* groups all possess at least one property in common which is responsible for their function as claimed². In addition, all of the recited *Markush* groups are directed to only portions of the claimed imidazole compounds not the entire

¹ Applicants respectfully direct the Examiner to In re Harnisch, 206 USPQ 300 (1980), wherein the Court of Customs and Patent Appeals stated that it was improper to reject a claim on the grounds that it is directed to an "improper *Markush* group". (In re Harnisch, 206 USPQ at 305) In view of In re Harnisch, the Examiner's rejection of claims 1, 2, 5, 7 and 14-18 for being drawn to an improper *Markush* group is improper and should be withdrawn.

² The members of *Markush* group contained in the definition of R¹ are all nitrogen-containing cyclic structures, i.e. imidazole, pyrrolidine, imidazole, triazoles etc.; the members of the *Markush* groups contained in the definitions of R², R³, R⁴, R⁵, R⁶, R⁸, R⁹, R¹¹, R¹², R²¹, R²⁴ and R²⁵ are all hydrocarbons; the members of the *Markush* group in the definition of R⁷, are H, =O, =S and several hydrocarbons; R²² contains a *Markush* groups directed to several thio groups and a -CO-containing member; and the *Markush* group of R³⁰ has a hydrocarbon, oxygen-, sulfur- or nitrogen-containing groups.

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 24

compound. "Where a *Markush* expression is applied only to a portion of a chemical compound, the propriety of the grouping is determined by a consideration of the compound as a whole, and does not depend on there being a community of properties in the members of the *Markush* expression." See MPEP §2173.05(h). Applicants assert that the *Markush* groups found in claims 1, 2, 5, 7 and 14-18 are recited in the conventional manner provided for in MPEP §2173.05(h) and that each member of each *Markush* group is fully supported in the disclosure as required by MPEP §608.01(p). Applicants further contend that the members of the recited *Markush* groups are sufficiently few in number thus requiring that the Examiner examine all members of the *Markush* groups in claims 1, 2, 5, 7 and 14-18, as required by MPEP §803.02, even though they may be directed to independent and distinct inventions.

In an effort to advance the prosecution of this application, however, Applicants are proceeding on the assumption that the Examiner intended to reject claims 1, 2, 5, 7 and 14-18 on the basis that said claims were directed to unelected inventions, see MPEP §706.03(m). In response thereto, the Applicants have amended claim 1 to limit the claimed compound to compounds containing an imidazobenzodiazepine ring. In particular, $n1 = 0$ has been deleted thus requiring that the central ring be a 7-membered

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 25

ring. In addition, it is now a requirement that R¹⁰ form a benzene ring with either R⁷ or R⁶. These amendments eliminate the possibility that the central ring is a 6-membered ring or that a benzene group is not fused to the central ring. Applicants submit that the instant application is now directed solely to Group I pursuant to the Restriction required by the Office Action mailed November 13, 2002 (Paper 7). Applicants respectfully request that the rejection of claims 1, 2, 5, 7 and 14-18 be reconsidered and withdrawn.

Applicants note that in the rejection of claims 1, 2, 5, 7 and 14-18 that the Examiner stated that the "different areas of fusion" was one basis for the restriction requirement which was not put forth in the November 13, 2002 Office Action as a basis for the restriction requirement. Applicants have, therefore, proceeded on the assumption that the Examiner did not intend on changing the basis for the restriction requirement in the instant Office Action, and as such, has not amended the claims to address this point. If this assumption is incorrect, Applicants respectfully contend that is improper for the Examiner to raise this basis in the present Office Action and that the finality of the restriction requirement was premature and must be rescinded so that a new, non-final Office Action directed solely to the new basis for a restriction can be issued to

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 26

allow Applicants the opportunity to appeal the Examiner's decision.

In an effort to advance the prosecution of this application, however, Applicants contend that the differing areas of fusion, with respect to the claimed compounds, do not support the further restriction of this application. In support thereof, Applicants respectfully request that the Examiner consider that when R¹⁰ is taken together with either R⁷ or R⁶ an imidazobenzodiazepine ring is formed. The separate inventions, identified as Group II, Group III and Group IV in the November 13, 2002 Office Action, are not, therefore, possible as the result of this amendment.

If the aforementioned assumptions are not correct, Applicants respectfully request clarification of the rejection contained in paragraph 3 of the instant Office Action.

4. Claims 15, 17 and 18 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

With respect to claim 15, the Examiner has failed to "point out wherein the indefiniteness resides," contrary to MPEP §707.07(d).

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 27

Without conceding the appropriateness of the Examiner's rejection of claims 17 and 18, and in an effort solely to advance the prosecution of the instant application, Applicants have canceled claims 17 and 18 without waiver or prejudice. Applicants respectfully request withdrawal of the rejection of claims 15, 17 and 18 under 35 U.S.C. §112, first paragraph, for all the reasons set forth above.

5. Claims 9, 10, 17 and 18 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which applicant [sic] regards as the invention.

a) - b) In response thereto, claim 9 has been amended to replace "Chloro" in line 8 with "chloro" and "Bromo" in line 10 with "bromo" and to delete "or" in line 13. Applicants respectfully submit that these amendments obviate the rejection of claim 9 under 35 U.S.C. 112, second paragraph.

c) - e) In response thereto, claim 10 has been amended to replace "Chloro" with "chloro" in line 6 and "Bromo" with "bromo" in line 8. In addition, Applicants have appended "or" to line 9, thus overcoming the rejection raised in paragraph 5(d) of the present Office Action. Finally, Applicants have appended the phrase "or a pharmaceutically acceptable salt thereof." to claim 10, thus

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 28

obviating the rejection raised by paragraph 5(e) of the present Office Action. Support for the former amendment is found in the description at page 14, lines 12-25. Applicants assert that none of the aforementioned amendments introduce new matter.

5.f)A. - 5.f)E. Without conceding the correctness of the rejection of claims 17 and 18 under 35 U.S.C. 112, second paragraph, as raised in paragraphs 5.f)A. to 5.f)E., Applicants have canceled claims 17 and 18 without waiver or prejudice. Applicants reserve the right to file a subsequent application directed to claims 17 and 18 at a later date. Applicants respectfully request withdrawal of the rejection of claims 9, 10, 17 and 18 under 35 U.S.C. §112, second paragraph, for all the reasons set forth above.

6. Claims 15-18 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 8-14 of co-pending application USSN 10/129,569. Applicants respectfully contend that claims 15 and 16 of the present application are patentability distinct from the claims of USSN 10/129,569. The present claims are directed to the treatment of a number of conditions, including several forms of cancer, related to the overproduction of prenyl transferase enzymes, by certain novel compounds discovered to inhibit such enzymes. The '569 application is directed

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 29

to the treatment of cancer with a composition comprised of at least one transduction inhibitor of heterotrimeric G protein signals combined with at least one other anti-cancer agent. It is well established that a combination of two known entities is patentable. As stated in MPEP §804, the analysis employed in an obviousness-double patenting determination parallels the guidelines for a 35 U.S.C. §103(a) rejection.

Applicants contend that the present application clearly does not teach, suggest or infer that a combination of the present compounds with a transduction inhibitor of heterotrimeric G protein signal, produces a therapeutic compound for the treatment of cancer. The '569 application does not teach or suggest the disclosure found at pages 16, line 6 to page 17, line 2, which enables one skilled in the art to practice claims 15 and 16. It should be noted that the MPEP suggests that double patenting is evidence when the subject application contains a disclosure which complies with 35 U.S.C. §112, second paragraph, for the claims of the co-pending application. Clearly claims 15 and 16 of the present application would be rejected under 35 U.S.C. §112, second paragraph, if combined with the disclosure of the '569 application and claims 1-6 and 8-14 of the '569 application would be rejected, under 35 U.S.C. §112, second

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 30

paragraph, if combined with the disclosure of the present application.

In an effort to simplify the prosecution of the instant application, however, Applicants have amended claim 15 to restrict the claimed pharmaceutical to the contested use, i.e. for the treatment of breast cancer, colon cancer, pancreas cancer, prostate cancer, lung cancer, ovarian cancer, epidermal cancer and hematopoietic cancer and added new claim 20 directed to a pharmaceutical composition used to treat the claimed non-cancerous conditions, i.e. fibrosis, benign prostatic hyperplasia, atherosclerosis, restenosis and hepatitis delta virus infections. Applicants contend that the subject matter of new claim 20 does not overlap with the subject matter of the claims from the '569 application. Applicants have amended claim 16 to delete the aforementioned non-cancerous conditions and have added new claim 21 directed to a method of treating such conditions by administering one of the novel compounds of claim 1. Like claim 20, claim 21 should not be subjected to the pending double patenting rejection. Applicants respectfully request the allowance of amended claims 15 and 16 as well as new claims 20 and 21.

Applicants have canceled claims 17 and 18, thus obviating the obviousness-type double patenting rejection

Inventor : Gordon et al.
Serial No. : 09/868,356
Filed : August 10, 2001
Page : 31

with respect to these claims. Applicants respectfully request the withdrawal of the rejection of claims 17 and 18.

7. Applicants acknowledge the objection to claims 12, 13 and 19 as being dependent upon a rejected base claim and appreciate the opportunity to amend said claims in independent form. Applicants respectfully decline the Examiner's invitation to amend said claims on the belief that the above amendments put the subject base claims in a condition for allowance. Applicants respectfully request that they be afforded the opportunity to amend claims 12, 13 and 19 at a later date if the Examiner finds that the amendments of the base claims do not overcome the stated rejections.

Applicants respectfully submit that the pending claims are in a condition for allowance and notification to that effect is earnestly solicited. Examiner Coleman is invited to telephone Applicant(s) attorney at (508) 478-0144 to facilitate prosecution of this application. Please apply any charges or credits to Deposit Account No. 50-0590 referencing attorney docket number 00537-188002.

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Biomeasure, Incorporated
27 Maple Street
Milford, MA 01757-3650
(508) 478-0144

Respectfully submitted,


Alan F. Feeney

Attorney for Applicant(s)
Reg. No. 43,609